REMARKS

Receipt of the Office Action mailed December 3, 2002 is acknowledged. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the remarks that follow.

Claims 19, 21, 28, and 30 are currently being amended. These amendments are not narrowing amendments related to patentability; rather, they are intended to be, and should be considered as, amendments to clarify the claims.

This amendment changes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 1-51 are pending in this application. Claims 1-14 and 35-51 are withdrawn from further consideration as being drawn to a non-elected invention. Claims 15-34 are currently under examination in this application. There are four rejections of record. First, claims 15-34 stand rejected under 35 U.S.C. § 112, ¶ 2, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Second, claims 15-34 stand rejected under 35 U.S.C. § 112, ¶ 1, as allegedly not being enabled for a method for using any vector DNA-coated with any metal carrying more than one antigen from more than one pathogenic viruses to induce an immune response in animals. Third, claims 15-19, 22-25, and 31-34 stand rejected as allegedly being unpatentable under 35 U.S.C. § 102. Finally, claims 15-34 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Johnston et al., United States Patent No. 6,194,389 B1 ("Johnston"), Braun et al. (Virology, 1999, Vol. 265, pp. 46-56) ("Braun"), Stanberry et al. (J. Infect. Dis. 1987, Vol. 155, pp. 914-20) ("Stanberry"), Pertmer et al. (Vaccine 1995, Vol. 13, pp. 1427-30) ("Pertmer"), and Barry et al. (Vaccine 1997, Vol. 15, pp. 788-91) ("Barry"). Applicants respectfully traverse these rejections. Applicants note with appreciation that the Office has withdrawn all other rejections.

35 U.S.C. § 112, ¶ 2

It is well settled that a claim term is not indefinite if "one skilled in the art would understand the bounds of the claim when read in light of the specification . . . ." *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001). For the reasons set forth below, it is respectfully submitted that the claims are clear and definite and that these rejections under 35 U.S.C. § 112, ¶ 2, should be withdrawn.

Derived

The Examiner rejected claims 15, 19, and 28, alleging that the term "derived" is indefinite. Applicants note that claims 19 and 28 do not recite the term "derived," but believe the Examiner intended to refer to claims 21 and 30, which do recite the term "derived." As a result, applicants will respond as if claims 15, 21, and 30 were rejected.

Applicants respectfully submit that the term "derived" should be given its ordinary meaning to one of skill in the art and that applicants have described the term consistently in the specification as "[a] sequence is 'derived or obtained from' a molecule if it has the same or substantially the same basepair sequence as a region of the source molecule, its cDNA, complement thereof or if it displays sequence identity" as further described in the specification. (See page 15, ll. 1-4) Applicants submit that the term is sufficiently clear and definite that one of ordinary skill in the art would understand the metes and bounds of the claim. As such, applicants respectfully request that the rejection be withdrawn.

Particle-Mediated Transdermal Technique

The Examiner further rejected claim 15, stating that the phrase "particle-mediated transdermal technique" is indefinite. Applicants begin by noting that the phrase in the claim is in fact "particle-mediated transdermal *delivery* technique." In response to the Examiner's inquiry whether a viral like particle is intended or a protein particle is intended, applicants submit that the claim limitation refers to a technique for administering the coated core carrier to the subject and does not refer to a particular particle.

Applicants again point to the specification, to illustrate the ordinary and customary meaning one of skill in the art would attribute to the phrase "particle-mediated transdermal

delivery technique." The instant specification points to United States Patent No. 5,865,796 (the "'796 patent") as evidence of the knowledge of those skilled in the art around the time the application was filed. (See page 11, ll. 2-5) The '796 patent describes particle-mediated acceleration of material into living cells and tissue and suggests that such techniques are known in the art. Moreover, the current specification describes "transdermal delivery" as intradermal, transdermal, and transmucosal administration (see page 10, ll. 24-27). In addition, it describes the use of a "core carrier" coated with a nucleic acid in order to impart a defined particle size as well as a sufficiently high density to achieve the momentum required for cell penetration, such that the DNA can be delivered using "particle-mediated delivery techniques," for example, those described in United States Patent No. 5,100,792. (See page 11, ll. 6-13) As a result, one of ordinary skill in the art would understand the ordinary meaning of the phrase "particle-mediated transdermal delivery technique." Applicants respectfully submit that this phrase is clear and definite and that one of ordinary skill in the art would understand the bounds of the claim. Applicants further request that this rejection be withdrawn.

An Amount Sufficient

The Examiner further rejected claim 15, stating that the phrase "an amount sufficient" is indefinite. Applicants respectfully request that the Examiner consider the phrase in context of the language of the claim of which is a part. The entire phrase used by the applicants in the claim is "an amount sufficient to elicit an immune response." Applicants point to the specification to illustrate the ordinary and customary meaning one of skill in the art would attribute to the phrase "an amount sufficient." Specifically, applicants point to page 36, ll. 2-19, page 37, ll. 23 through page 38, ll. 1, and page 41, ll. 1-20. The specification describes the amount sufficient in the same manner as the claim, as an amount that will elicit an immune response. It further acknowledges that this amount will fall into a broad range, but that the amount sufficient can be readily determined by one of skill in the art through routine trials. (See page 37, ll. 23-29 and page 38, ll. 1-9) As such, applicants respectfully submit that "one skilled in the art would understand the bounds of the claim when read in light of the specification . . . ." *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001).

At Least One Pathogen

The Examiner rejected claims 19 and 28, stating that the recitation "the vector construct comprises at least one pathogen" is unclear. Since claim 15 recites "vector constructs comprising genomic DNA fragments derived or obtained from one or more pathogens," a requirement that at least one of the pathogens be a virus is not indefinite or unclear to one of skill in the art. The Examiner further states that claims 19 and 28 do not provide an upper-limitation of the intended composition.

Without acquiescing in the rejection and without intending to abandon claimed subject matter but to expedite allowance, claims 19 and 28 have been amended. As stated above, applicants believe these amendments are not narrowing amendments related to patentability. Rather, they are intended to be, and should be considered as, amendments to clarify the meaning of claim 19 and claim 28. As stated in response to previous office actions, the ordinary skilled artisan understands that a plasmid vector can have up to about 25 kilobases of guest nucleic acids and that a cosmid vector ranges from about 25 kilobases to about 50 kilobases of guest nucleic acids and that exceeding the upper limits result in unstable molecules. As a result, these claims are not narrowed by the current amendment. As such, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

More Than One Virus

The Examiner rejected claims 21 and 30, stating that the recitation "more than one virus" does not provide an upper-limitation of the intended composition. Again, the Examiner states that the claim should point out the upper limitation of the pathogen.

Without acquiescing in the rejection and without intending to abandon claimed subject matter but to expedite allowance, claims 21 and 30 have been amended. As stated above, applicants believe these amendments are not narrowing amendments related to patentability. Rather, they are intended to be, and should be considered as, amendments to clarify the meaning of claim 21 and claim 30. As stated in response to previous office actions, the ordinary skilled artisan understands that a plasmid vector can have up to about 25 kilobases of guest nucleic acids and that a cosmid vector ranges from about 25 kilobases to

about 50 kilobases of guest nucleic acids and that exceeding the upper limits result in unstable molecules. As a result, these claims are not narrowed by the current amendment.

A Density Sufficient

The Examiner rejected claims 22 and 31, stating that the recitation "a density sufficient" is not defined. Applicants point to the specification to illustrate the ordinary and customary meaning one of skill in the art would attribute to the phrase "a density sufficient." Specifically, applicants point to page 4, ll. 1-12, page 11, ll. 6-13, and page 38, l. 28 through page 40, l. 7. The specification teaches that the sufficiency of the density will depend on the distance one desires the particle to penetrate a target surface. (See page 39, ll. 11-20) The specification also teaches an optimal density and a sufficient density for the desired effect can be readily determined by one of skill in the art through routine trials. As such, applicants respectfully submit that one skilled in the art would understand the bounds of the claim when read in light of the specification.

A Metal

Finally, the Examiner rejected claims 23 and 32 under 35 U.S.C. § 112, ¶ 2, stating that the recitation of "a metal" is not defined. Applicants respectfully submit that one of skill in the art would understand the meaning of the term "a metal." As such, applicants respectfully request that this term be given its ordinary meaning. In addition, applicants reiterate that they point to the specification to illustrate the ordinary and customary meaning one of skill in the art would attribute to the term "a metal," as defined herein. Specifically, applicants point to page 8, ll. 1-7 and page 33, ll. 22 through page 34, ll. 14. The specification teaches tungsten, gold, platinum, and iridium as examples of metals that can be used in accordance with this invention. (See page 34 ll. 4-5) Those of ordinary skill in the art would know which other metals can also be used in accordance with this invention. In sum, applicants respectfully submit that one skilled in the art would understand the bounds of the claims when read in light of the specification.

35 U.S.C. § 112, ¶ 1

The Examiner rejected claims 15-34, stating that, while the specification enables a method for using a vector DNA coated with gold particle carrying only one antigen of a HSV glycoprotein D to induce immune response in an animal, it does not enable a method for using any vector DNA-coated with any metal carrying more than one antigen from more than one pathogenic viruses to induce an immune response in animals. Applicants respectfully reiterate that the claims recite a method employing a core carrier that is coated with vector constructs comprising genomic DNA fragments. The genomic DNA fragments are not required to be coated with gold particles. Applicants respectfully traverse this rejection.

35 U.S.C. § 112 ¶ 1 states: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . ." Under this standard, applicants must provide a specification that enables a person reasonably skilled in the art to make and use the claimed invention without undue experimentation. The fact that some experimentation may be employed, however, does not make it undue if a person of skill in the art typically engages in such experimentation. This is because the prohibition is against "undue experimentation," not merely "experimentation." *In re Angstadt,* 537 F.2d 498, 502- 03 (CCPA 1976).

As presented previously, the specification discloses and enables more than the narrow HSV glycoprotein D to induce immune response in an animal. (See Examples at page 41-49) The Examples describe the assembly of numerous different antigen constructs that have been assembled according to the claimed invention and then demonstrate that these constructs have the recited features in working, art-recognized animal model systems. In Example 1, six different cosmid constructs were made, each containing different EcoR1 restriction genomic fragments from HSV-2, which were administered to mice in an art-recognized model and established to induce the desired immune response. (See page 46, ll. 6-16) In Example 2, a plasmid construct was made containing 8500bp of HSV-2 DNA (including genomic sequences encoding glycoprotein B protein antigen) and this construct was administered to

mice in an art-recognized model and established to induce the desired immune response. (See page 48, ll. 26-29)

The specification also describes several additional antigens that can be included in the genomic DNA sequences; where to find the sequence information for such antigens; how to go about obtaining the sequences; how to select appropriate control sequences; how to produce an appropriate expression cassette; how to insert the expression cassettes into numerous different vector constructs; and how to administer these vector constructs to obtain expression of the antigens of interest. As an example, the specification discloses various HIV antigens, various antigens derived from the hepatitis family of viruses and from the herpes simplex viruses, and antigens from many additional viral, bacterial, and parasitic sources. (See also pages 20-23) It also fully describes how to prepare genomic libraries (see pages 24-27) and how to coat and administer a core carrier with vector constructs (see pages 33-36). Requiring applicants to provide an exhaustive experimental study into any and all possible embodiments would discourage disclosure of discoveries and is in direct contradiction of the principles underlying 35 U.S.C. § 112. *See, e.g., Rohm & Haas Co. v. Dawson Chemical Co.*, 217 USPQ 515, 563-64 (S.D. Tex. 1983), *rev'd on other grounds*, 220 USPQ 289 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). Applicants have shown that their invention is fully operative across a wide variety of different constructs. There is no reason to doubt that applicants' compositions will be suitable for use with other pathogens or with multiple pathogens.

In addition, the specification describes several metals, besides gold, that can be used in accordance with this invention. (See page 34 ll. 4-5) The specification teaches tungsten, gold, platinum, and iridium as examples of metals that can be used in accordance with this invention. (See page 34 ll. 4-5) Those of ordinary skill in the art would know which other metals can also be used in accordance with this invention. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991) (*quoting In re Angstadt;* 537 F.2d 498, 502- 03 (CCPA 1976)). Therefore, applicants respectfully submit that they have provided sufficient disclosure to enable one of skill in the art to make and use the invention commensurate with the scope of the claims. Finally, the fact that some metals

exhibit toxicity does not mean that they would not function in accordance with the invention. Applicants respectfully submit that it would therefore be improper and unnecessary to limit the claims to the metal, gold.

35 U.S.C. § 102

It is well settled that a determination that a patent is invalid as being anticipated under 35 U.S.C. § 102 requires a finding that "each and every limitation is found either expressly or inherently in a single prior at reference." *Celeritas Techs. Inc. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1360, 47 USPQ2d 1516, 1522 (Fed. Cir. 1998). For the reasons set forth below, the claims are not anticipated by the prior art of record.

Braun (Virology, 1999, Vol. 265, pp. 46-56)

The Examiner rejected claims 15-19, 22-25, and 31-34 under 35 U.S.C. § 102(a) as allegedly being unpatentable over Braun. Applicants direct the Examiner's attention to the date of publication of Braun, December 5, 1999 (See APPENDIX A). Since the present application claims priority to US Provisional Application Serial No. 60/163,297, which was filed on November 3, 1999, applicants submit that Braun is not a proper 35 U.S.C. § 102(a) prior art reference. Applicants therefore respectfully request that the rejection based on Braun be withdrawn.

Braun, nevertheless, fails to anticipate claims 15-19, 22-25, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Braun fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Braun does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of claims 15-19, 22-25, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

Tacket et al. (Vaccine 1999, Vol. 17, pp. 2826-29)

The Examiner rejected claims 15, 17-19, 22-28, and 31-34 under 35 U.S.C. § 102(a) as allegedly being unpatentable over Tacket et al. (Vaccine 1999, Vol. 17, pp. 2826-29) ("Tacket"). In particular, the Examiner asserts that Tacket discloses the same method of using a metal particle-mediated DNA immunization delivered by a particle mediated transdermal delivery system, PowderJect XR1, onto the skin of a human to induce a booster response against Hepatitis B. Applicants respectfully traverse this rejection.

Tacket fails to anticipate claims 15, 17-19, 22-28, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Tacket fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Tacket does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of claims 15, 17-19, 22-28, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

Lodmell et al. (Vaccine 1998, Vol. 16, pp. 115-118)

The Examiner rejected claims 15, 17-19, 22-28, and 31-34 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Lodmell et al. (Vaccine 1998, Vol. 16, pp. 115-118) ("Lodmell"). In particular, the Examiner asserts that Lodmell discloses the same method of using a metal particle-mediated DNA immunization delivered by a particle mediated transdermal delivery system to induce an immune response against viral antigen of glycoprotein G. Applicants respectfully traverse this rejection.

Lodmell fails to anticipate claims 15, 17-19, 22-28, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Lodmell fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Lodmell does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of

claims 15, 17-19, 22-28, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

Haynes et al. (AIDS Research and Human Retroviruses 1994, Vol. 10, pp. S43-S45)

The Examiner rejected claims 15, 17-19, 22-28, and 31-34 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Haynes et al. (AIDS Research and Human Retroviruses 1994, Vol. 10, pp. S43-S45) ("Haynes"). In particular, the Examiner asserts that Haynes discloses the same method of using a metal particle-mediated DNA immunization delivered by a particle mediated transdermal delivery system to induce an immune response against viral antigen of HIV gp160 and gp120. Applicants respectfully traverse this rejection.

Haynes fails to anticipate claims 15, 17-19, 22-28, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Haynes fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Haynes does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of claims 15, 17-19, 22-28, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

Webster et al. (Vaccine 1994, Vol. 12, pp. 1495-98)

The Examiner rejected claims 15, 17-19, 22-28, and 31-34 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Webster et al. (Vaccine 1994, Vol. 12, pp. 1495-98) ("Webster"). In particular, the Examiner asserts that Webster discloses a metal coated vector construct that is gold coated plasmid DNA, which expresses an influenza virus haemagglutinin and IL-2 of a vector DNA construct encoding a viral antigen. Applicants respectfully traverse this rejection.

Webster fails to anticipate claims 15, 17-19, 22-28, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce

an immune response. Webster fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Webster does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of claims 15, 17-19, 22-28, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

Macklin et al. (Journal of Virology 1998, Vol. 72, pp. 1491-96)

The Examiner rejected claims 15, 17-19, 22-28, and 31-34 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Macklin et al. (Journal of Virology 1998, Vol. 72, pp. 1491-96) ("Macklin"). In particular, the Examiner asserts that Macklin discloses a metal coated DNA vector construct that is gold coated plasmid DNA vector carrying viral antigen of influenza virus HA protein to induce an immune response. Applicants respectfully traverse this rejection.

Macklin fails to anticipate claims 15, 17-19, 22-28, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Macklin fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Macklin does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of claims 15, 17-19, 22-28, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

Fynan et al. (P.N.A.S. U.S.A. 1993, Vol. 90, pp. 11478-82)

The Examiner rejected claims 15, 17-19, 22-28, and 31-34 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Fynan et al. (P.N.A.S. U.S.A. 1993, Vol. 90, pp. 11478-82) ("Fynan"). In particular, the Examiner asserts that Fynan discloses a metal coated DNA vector construct that is gold coated plasmid DNA vector carrying viral antigen of influenza virus HA1 protein to induce an immune response. Applicants respectfully traverse this rejection.

Fynan fails to anticipate claims 15, 17-19, 22-28, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Fynan fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Fynan does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of claims 15, 17-19, 22-28, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

United States Patent No. 6,194,389 (Johnston et al.)

The Examiner rejected claims 15, 17-19, 22-28, and 31-34 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Johnston. Applicants respectfully traverse this rejection. Applicants direct the Examiner's attention to the date of issue of the Johnston patent, February 27, 2001. Since the present application claims priority to US Provisional Application Serial No. 60/163,297, which was filed on November 3, 1999, applicants submit that Johnston is not a proper section 102(b) prior art reference. Applicants also note that the patent application leading to the Johnston patent was not published under 35 U.S.C. § 122(b) during its pendency at the PTO. Applicants respectfully request that the 35 U.S.C. § 102(b) rejection based on Johnston be withdrawn.

Johnston, nevertheless, fails to anticipate claims 15, 17-19, 22-28, and 31-34 because it does not disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Johnston fails to disclose a construct containing a genomic fragment that is greater than 5 kilobases in size. As a result, Johnston does not disclose each and every limitation of the claims as required under 35 U.S.C. § 102. For these reasons, the rejection of claims 15, 17-19, 22-28, and 31-34 is improper and reconsideration and withdrawal is respectfully requested.

35 U.S.C. § 103(a)

The Examiner rejected claims 15-34 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Johnston, Braun, Stanberry, Pertmer, or Barry. In particular, the Examiner asserts that the references all relate to a metal, gold coated vector DNA construct that encodes a viral antigen, where some of the antigens have a similar size as that disclosed in the current application, for example, glycoprotein of herpes virus. Further, the Examiner asserts that lots of eukaryotic vectors and plasmids are able to carry a large sized insert. The Examiner goes on to conclude that the method for using a gene gun for delivering a DNA-coated particle loaded with a DNA plasmid for inducing an immune response is a well established method with more efficient effect and economically beneficial and, absent unexpected results, the modification of the plasmid carrying more than one antigens either from the same pathogenic virus or from different pathogenic viruses in a certain size is generally recognized as being within the level of ordinary skill in the art. Applicants respectfully traverse this rejection.

As discussed in the previous section, applicants submit that Braun, published on December 5, 1999, is not a section 102(a) prior art reference to the present application, which application claims priority to US Provisional Application Serial No. 60/163,297, filed on November 3, 1999. As a result, it is also not proper prior art reference for the purposes of section 103(a). In addition, it is noted that Johnston, which issued on February 27, 2001 is not a 102(b) reference to the present application.

Section 2143 of the MPEP sets forth the following three basic requirements for *prima facie* obviousness: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. When assessing these issues, (1) the claimed invention must be considered as a whole; (2) the references must be considered as a whole and must suggest the desirability of making the combination; (3) the references must be viewed without the benefit of impermissible hindsight; and (4) a reasonable expectation of success is the standard with which obviousness is determined. Hodosh v. Block Drug Co.,

Inc., 229 USPQ 182, 187 n. 5 (Fed. Cir. 1986). Applicants submit that the Office has failed to satisfy these criteria and thus has failed to establish a *prima facie* case of obviousness.

Applicants respectfully submit that Johnston, Braun, Stanberry, Pertmer, and Barry do not disclose or teach all of the limitations of the presently claimed invention as set forth in claim 15 and that the modification suggested by the Examiner would not have rendered the pending claims obvious at the time the invention was made to a person having ordinary skill in the art. As such, claim 15 is patentable over this combination of references. Since claims 16-34 are dependent from claim 15, for at least this reason claims 16-34 are patentable over the prior art of record.

None of the cited references disclose or suggest, either explicitly or inherently, a method where the vector constructs contain genomic fragments "greater than 5 kilobases in size" and are administered to produce an immune response. Rather, the Examiner proffers a blanket statement that lots of eukaryotic vectors and plasmids are able to carry a large sized insert; however, the Examiner provides no support for this statement. Moreover, the Examiner states that none of the prior art references disclose limiting the DNA to less than 5 kilobases in size. Applicants submit that it is precisely the fact that the prior art references do not disclose that the DNA is greater than 5 kilobases in size that results in the failure to render the claims obvious. As such, the references fail to teach or suggest all of the applicants' claim limitations. Moreover, none of the references provide any motivation to modify the methods disclosed in the references to genomic DNA fragments that are greater than 5 kilobases in size. Thus, the PTO has failed to establish its showing of *prima facie* obviousness.

Furthermore, none of the references, Johnston, Braun, Stanberry, Pertmer, or Barry, disclose a method where the genomic DNA fragments are derived from more than one virus as recited in claims 21 and 30. This is not generally recognized as being within the skill in the art. The Examiner provides no evidence to support an assertion that this is known in the art and cites no references that suggest that such a modification was within the skill in the art. Finally, Stanberry does not disclose administering a coated core carrier to the subject using a particle-mediated transdermal delivery device and therefore would not likely be combined

with the other cited references. Again, the PTO has failed to establish its showing of *prima facie* obviousness. Reconsideration and withdrawal of the rejections of claims 15-34 over the combination of Johnston, Braun, Stanberry, Pertmer, or Barry is respectfully requested.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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